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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/565,453

05/18/2006

Johann Zimmermann

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9886

1095

7590

05/14/2008

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER

STONE, CHRISTOPHER R

ART UNIT

PAPER NUMBER

1614

MAIL DATE

DELIVERY MODE

05/14/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/565,453	Applicant(s) ZIMMERMANN ET AL.	
	Examiner CHRISTOPHER R. STONE	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 March 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 5 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/18/2006</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election of 2-(imidazol-1-yl)-1-hydroxyethane-1,1-diphosphonic acid (zoledronic acid) and N-[2-cyano-4-(2,2-dimethyl-propylamino)-pyrimidin-5-ylmethyl]-4-(4-methyl-piperazin-1-yl) benzamide in the reply filed on December 19, 2007 is acknowledged. Applicant's election of bone metastasis in the reply filed on March 25, 2008 is acknowledged.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of bone metastasis, does not reasonably provide enablement for the prevention or prophylaxis of bone metastasis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 1-3 are drawn to a method of treating bone metastasis comprising administering 2-(imidazol-1-yl)-1-hydroxyethane-1,1-diphosphonic acid (zoledronic acid)

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and N-[2-cyano-4-(2,2-dimethyl-propylamino)-pyrimidin-5-ylmethyl]-4-(4-methyl-piperazin-1-yl) benzamide. Page 4 of the instant specification defines treatment to include prophylactic and preventative treatment. The prior art indicates that cancer is difficult to prevent. No single chemotherapeutic drug is useful for the prevention of every case of cancer. In fact, some cancers do not respond well to any known chemotherapeutic drugs (see Oxford Textbook of Oncology, p. 451, Column 2, last paragraph). These negative results indicate a lack of predictability in the art. Furthermore, the Applicant has provided no working examples demonstrating the ability of the instantly claimed method to prevent bone metastasis. For these reasons, it would take undue experimentation by one of ordinary skill in the art to use this method to treat cancers, other than ovarian cancer, with a reasonable expectation of success.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

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consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okuno et al (US PG PUB 2002/0142996) in view of Altman et al (WO 03/020278).

Claims 1-3 and 5 are drawn to a composition comprising 2-(imidazol-1-yl)-1-hydroxyethane-1,1-diphosphonic acid (zoledronic acid) and N-[2-cyano-4-(2,2-dimethyl-propylamino)-pyrimidin-5-ylmethyl]-4-(4-methyl-piperazin-1-yl) benzamide and a method of treating bone metastasis comprising administering said composition.

Okuno et al (US PG PUB 2002/0142996) teaches a method of treating bone metastasis comprising administering zoledronic acid (abstract and paragraph [0009]. Okuno et al does not teach the method/composition further comprising N-[2-cyano-4-(2,2-dimethyl-propylamino)-pyrimidin-5-ylmethyl]-4-(4-methyl-piperazin-1-yl) benzamide. Altman et al teaches N-[2-cyano-4-(2,2-dimethyl-propylamino)-pyrimidin-5-ylmethyl]-4-(4-methyl-piperazin-1-yl) benzamide is useful in the treatment of tumor metastasis (p. 21, compound I-2 and p. 14 lines 1-8). Applicant is reminded of in re Kerkhoven which affirmed that "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) Therefore it would have been obvious to one of ordinary skill in the art at the time of the instant application to combine zoledronic acid and N-[2-cyano-4-(2,2-dimethyl-propylamino)-pyrimidin-5-

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ylmethyl]-4-(4-methyl-piperazin-1-yl) benzamide into a single composition and to administer said composition to a patient to treat bone metastasis, since zoledronic acid was known to be useful for treating bone metastasis and N-[2-cyano-4-(2,2-dimethyl-propylamino)-pyrimidin-5-ylmethyl]-4-(4-methyl-piperazin-1-yl) benzamide was known to be useful for treating metastasis in general (i.e. the compounds were known to be useful for the same purpose), thus resulting in the practice of the instantly claimed invention with a reasonable expectation of success.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER R. STONE whose telephone number is (571)270-3494. The examiner can normally be reached on Monday-Thursday, 7:30am-4:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

28April2008

CRS

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614